

Amendments to the claims:

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

1. *(original)* A method for assessing the potential of a compound to function as an anti-arrhythmic agent comprising:
 - (a) providing a cell that expresses a recombinant mutant Nav1 sodium channel protein;
 - (b) measuring a first plateau current in said cell;
 - (c) exposing said cell to a test compound;
 - (d) measuring a second plateau current in said cell; and
 - (e) comparing said first and second currents whereby a lower second current indicates that said test compound is a potential anti-arrhythmic agent;said mutant sodium channel protein having an amino acid sequence in which one or more amino acids among the ten amino acids occurring at the carboxy end of the S6 segments of D1, D2, D3 or D4 domains of a mammalian Nav1 protein differs from the amino acid in wild-type Nav1 by substitution with tryptophan, phenylalanine, tyrosine or cysteine.
2. *(original)* The method of claim 1 wherein said mammalian Nav 1 protein is selected from Nav 1.1, Nav 1.2, Nav 1.3, Nav 1.4, Nav 1.5, Nav 1.6, Nav 1.7, or Nav 1.8.
3. *(original)* The method of claim 2 wherein said mammalian Nav 1 protein is Nav 1.4 or Nav 1.5.
4. *(original)* A method for assessing the potential of a compound as an anti-arrhythmic agent comprising:
 - (a) providing a cell that expresses a recombinant mutant Nav1 sodium channel protein;
 - (b) measuring a first plateau current in said cell;

(c) exposing said cell to a test compound;
(d) measuring a second plateau current in said cell; and
(e) comparing said first and second currents whereby a lower second current indicates that said test compound is a potential anti-arrhythmic agent;
said mutant sodium channel protein having an amino acid sequence in which at least one amino acid chosen from amino acids 19, 21 and 22 of the S6 segment of D1 and amino acids 23 and 24 of the S6 segment of the D4 domain of a mammalian Nav1 protein differs from the amino acid in wild-type Nav1 by substitution with tryptophan, phenylalanine, tyrosine or cysteine.

5. **(original)** The method of claim 4 wherein said mammalian Nav 1 protein is selected from Nav 1.1, Nav 1.2, Nav 1.3, Nav 1.4, Nav 1.5, Nav 1.6, Nav 1.7, or Nav 1.8.

6. **(original)** The method of claim 5 wherein said mammalian Nav 1 protein is Nav 1.4 or Nav 1.5.

7. **(original)** A method for assessing the potential of a compound as an anti-arrhythmic agent comprising:

(a) providing a human cell that expresses a recombinant mutant Nav1.4 or Nav1.5 sodium channel protein;
(b) measuring a first plateau current in said cell;
(c) exposing said cell to a test compound;
(d) measuring a second plateau current in said cell; and
(e) comparing said first and second currents whereby a lower second current indicates that said test compound is a potential anti-arrhythmic agent;
said mutant sodium channel protein having an amino acid sequence in which at least one amino acid chosen from amino acids L435, L437, A438, I1589 and I1590 of wild-type rNav1.4 is replaced by tryptophan, phenylalanine or tyrosine, or in the case of L437 additionally with cysteine.

8. **(original)** A method according to claim 1 wherein said cell is chosen from a human embryonic kidney cell and a Chinese hamster ovary cell.
9. **(original)** A method according to claim 1 wherein one or more wild-type amino acids are replaced with tryptophan.
10. **(original)** A method according to claim 3 wherein the mammalian Nav1.4 or Nav1.5 is rat or human Nav1.4 or Nav1.5 and a leucine corresponding to L437 of rNav1.4 is replaced with cysteine.
11. **(original)** A method according to claim 10 wherein L437 is replaced with cysteine and one or both of a leucine and an alanine corresponding to L435 and A438 respectively of rNav1.4 are replaced with tryptophan.
12. **(original)** The method according to claim 3 wherein the mammalian Nav1.4 or Nav1.5 is rat or human Nav1.4 or Nav1.5.
13. **(original)** The method according to claim 12 wherein an alanine corresponding to A438 and an isoleucine corresponding to I1589 in rNav1.4 are replaced.
14. **(original)** The method according to claim 13 wherein said alanine and isoleucine are replaced by tryptophan.
- 15-30. **(cancelled)**
31. **(original)** A screen for assessing the potential of a compound to treat a pathological condition manifested by an increased late sodium current in a heart comprising:
- (a) providing a cell that expresses a recombinant mutant Nav1 sodium channel protein;
 - (b) measuring a first plateau current in said cell;
 - (c) exposing said cell to a test compound;

(d) measuring a second plateau current in said cell; and
(e) comparing said first and second currents whereby a lower second current indicates that said test compound is a potential anti-arrhythmic agent;
said mutant sodium channel protein having an amino acid sequence in which one or more amino acids among the ten amino acids occurring at the carboxy end of the S6 segments of D1, D2, D3 or D4 domains of mammalian Nav1 differs from the amino acid in wild-type Nav1 by substitution with tryptophan, phenylalanine, tyrosine or cysteine.

32. *(original)* The method of claim 31 wherein said mammalian Nav1 protein is selected from Nav 1.1, Nav 1.2, Nav 1.3, Nav 1.4, Nav 1.5, Nav 1.6, Nav 1.7, or Nav 1.8.

33. *(original)* The method of claim 32 wherein said mammalian Nav 1 protein is Nav 1.4 or Nav 1.5.

34. *(original)* A screen for assessing the potential of a compound to treat a pathological condition manifested by an increased late sodium current in a heart comprising:
(a) providing a cell that expresses a mutant Nav1 sodium channel protein;
(b) measuring a first plateau current in said cell;
(c) exposing said cell to a test compound;
(d) measuring a second plateau current in said cell; and
(e) comparing said first and second currents whereby a lower second current indicates that said test compound is a potential anti-arrhythmic agent;
said mutant sodium channel protein having an amino acid sequence in which at least one amino acid chosen from amino acids 19, 21 and 22 of the S6 segment of D1 and amino acids 23 and 24 of the S6 segment of the D4 domain of mammalian Nav1.4 or Nav1.5 differs from the amino acid in wild-type Nav1 by substitution with tryptophan, phenylalanine, tyrosine or cysteine.

35. *(original)* The method of claim 34 wherein said mammalian Nav1 protein is selected from Nav 1.1, Nav 1.2, Nav 1.3, Nav 1.4, Nav 1.5, Nav 1.6, Nav 1.7, or Nav 1.8.

36. **(original)** The method of claim 35 wherein said mammalian Nav 1 protein is Nav 1.4 or Nav 1.5.

37. **(original)** A screen for assessing the potential of a compound to treat a pathological condition manifested by an increased late sodium current in a heart comprising:

(a) culturing a human cell that produces mutant Nav1.4 or Nav1.5 sodium channel protein;

(b) measuring a first plateau current in said cell;

(c) exposing said cell to a test compound;

(d) measuring a second plateau current in said cell; and

(e) comparing said first and second currents whereby a lower second current indicates that said test compound is a potential anti-arrhythmic agent;

said mutant sodium channel protein having an amino acid sequence in which at least one amino acid chosen from amino acids L435, L437, A438, I1589 and I1590 of wild-type rNav1.4 is replaced by tryptophan, phenylalanine or tyrosine, or in the case of L437 additionally with cysteine.

38. **(original)** A screen according to claim 34 wherein said cell is chosen from a human embryonic kidney cell and a Chinese hamster ovary cell.

39. **(original)** A screen according to claim 34 wherein one or more wild-type amino acids are replaced with tryptophan.

40. **(original)** A screen according to claim 34 wherein the mammalian Nav1.4 or Nav1.5 is rat or human Nav1.4 or Nav1.5 and a leucine corresponding to L437 of rNav1.4 is replaced with cysteine.

41. **(original)** A screen according to claim 40 wherein L437 is replaced with cysteine and one or both of a leucine and an alanine corresponding to L435 and A438 respectively of rNav1.4 are

replaced with tryptophan.

42. (*original*) A screen according to claim 34 wherein the mammalian Nav1.4 or Nav1.5 is rat or human Nav1.4 or Nav1.5.

43. (*original*) A screen according to claim 42 wherein an alanine corresponding to A438 and an isoleucine corresponding to I1589 in rNav1.4 are replaced.

44. (*original*) A screen according to claim 43 wherein said alanine and isoleucine are replaced by tryptophan.

45. (*original*) A screen according to claim 34 wherein said mutant sodium channel protein gives rise to sodium channels exhibiting plateau currents of greater than 1 nanoamp.